

ADDITIONAL FEES

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REMARKS

Claims 1-3, 5 and 11-16 are in the application. New claims 17- , have been added.

Applicants note with gratitude the concise comments in the Advisory Action. The suggestions asserted therein have been adopted, and it is believed that the claims are in condition for allowance.

Responses to the Advisory Action of August 9, 2002

The new and amended claims have been drafted to more clearly reflect the coverage of elected species — i.e., free radical scavengers. The proteins/peptides now expressly indicate that this activity is required in the claimed hydrogel. See Examiner's point (1), and NOTE on page 1 of action.

Claim 17 includes a limitation reflecting that the matrix is diisocyanato-PEG, thus including a structural property that reflects the basis of the much more rapid gelling times. See discussion of Examiner's point (3).

Thus, it suggested that the claim will not require any additional search, and that the claims are in condition for allowance.

Point (1) in Advisory Action, Page 2.

Examiner has stated that our arguments against Fortier are irrelevant because the claimed hydrogels have no limitations indicating “the absence of BSA.”

In accordance with Examiner’s suggestion to incorporate a limitation reflecting the absence of BSA, new claim 17 is presented.

New claim 17 requires that *the attachment of the catalytically active peptides or proteins to the PEG matrix is neither dependent on, nor mediated by the presence of catalytically inactive peptides, proteins or polymer species.*

The bold italics refer to the requirement of direct attachment of catalytically active proteins in the absence of catalytically inactive proteins – of which BSA is a member. A novel feature of the present invention is that the catalytic proteins are directly linked to the PEG. Therefore, the claimed hydrogel does not need BSA to serve as a mediator for protein attachment – i.e., cross-link proteins.

In addition, the claimed hydrogel does not require *any* non-catalytic or structural protein, and therefore the scope of the claim may properly reflect the complete independence from structural (i.e., non-catalytic) proteins.

Point (2) in Advisory Action, Page 2.

Applicants believe that the foregoing amendments render the rejections over Fortier/Galin moot. However, in the case that Examiner does not concur, we respectfully disagree with Examiner that Galin with Fortier render the claims obvious in view of claim 17, the foregoing remarks, and the following discussion of Galin.

Briefly, Galin is not an enabling reference to create a PEG hydrogel having covalently attached active enzymes.

In order for a reference to be enabling, one of ordinary skill in the art must be able to combine the teachings of Galin and Fortier with his or her own knowledge to create the claimed invention. *In re Donohue*, 226 USPQ 619 (Fed. Cir. 1985), cited in MPEP § 2141.02.

Galin would be enabling for creating copolymerized matrices comprising PEG and urethane groups. There is no teaching for the applicability to other uses.

However, the invention is not merely a PEG matrix copolymerized with an isocyanate as is the case with Galin. The claimed hydrogel possesses active enzymes complexed directly to the PEG, something that Fortier does not disclose. Nor does he disclose or suggest that an isocyanate would achieve the result claimed herein. Thus, there is no motivation to combine the references because there is no reasonable expectation of success. Only with hindsight inspection of the Applicants' specification would one in the art approximate the instant claims. This would be an entirely improper mode of analysis.

"A reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention." *In re Donohue*, supra. Applicants respectfully suggest that the public was not in possession of the claimed hydrogels.

This is even further supported by the '955 patent to Gould et al. Examiner cites this patent to demonstrate that isocyanates were known in the art "for the activation of PEG." But neither Gould nor Galin's polymers are "*activated*." The polymers are never reacted subsequent to polymer formation. Gould's gels are used as dried polymers, that swell in a solution of an agent. These gels do not bind anything, they merely entrap fluid, like e.g., a chromatograph matrix or polyacrylamide gel. See Gould's examples.

This does not resemble a key feature of the claims.

Examiner is correct in pointing out that it was known that isocyanates react with PEG to form copolymers. And that these copolymers may be either crystallized (Galin) or swelled in a solvent to absorb a quantity of solution (Gould). But neither reference, even with Fortier hint that one could use isocyanates with Fortier's PEG to reach a hydrogel comprising covalently attached and active enzymes.

It is respectfully suggested that Examiner still views the claimed hydrogel as merely a mixture of PEG and isocyanate, similar to that described in her previously proposed claim.

Applicants respectfully request withdrawal of the rejection under § 103(a) in view of the remarks and the amendments.

Point (3) of the Advisory Action

Examiner states that claim 1 must include a recitation of unexpected results. This is clearly incorrect. There is no requirement to include gelling times in claim 17. Unexpected results comprise objective evidence that the claimed and referenced inventions are different, and are not required to appear in the claims *per se*.

Perhaps Examiner is suggesting that a structural limitation be included in claim 17 in order to disclose the property of the claimed hydrogel that contributes to the gelling time.

To this end, the new claim 17 recites the matrix as being a diisocyanato-PEG. One with skill in the art would clearly appreciate that PEG and a diisocyanate must be the starting reagents.

In accordance with adopting this suggestion, Applicants respectfully request that the new claims be allowed and the application be passed to issuance.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read "Theodore A. Gottlieb", written over a horizontal line.

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